UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,357	07/13/2006	Moshe Baru	27048U	1205

20529 7590 03/28/2008

NATH & ASSOCIATES
112 South West Street
Alexandria, VA 22314

EXAMINER	
HA, JULIE	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
03/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,357	BARU ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-52* is/are pending in the application.

4a) Of the above claim(s) *44,45.48,49 and 52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-43,46,47,50,51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/04/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final rejection filed January 04, 2008 is acknowledged. Claims 28-52 are pending in this application. Applicant elected without traverse of species G-CSF for protein and multiple sclerosis as the disease in the reply filed on June 11, 2007. Claims 44-45, 48-49 and 52 remain withdrawn from further consideration as being drawn to nonelected species. Claims 28-43, 46-47 and 50-51 are examined on the merits in this office action.

Declaration under 37 CFR 1.132

1. Declaration under 37CFR 1.132 filed on January 04, 2008 has been considered.

Withdrawn Objection and Rejection

2. Objection to the title is hereby withdrawn due to Applicant's arguments.

3. Rejections under 35 U.S.C. 103(a) are hereby withdrawn due to Applicant's persuasive arguments.

Maintained Rejection

35 U.S.C. 112, 1st

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 47, 50 and 51 are rejected are under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for hemophilia, does not reasonably provide enablement for any other diseases, disorder or conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention is drawn to a method of treatment of a patient suffering from a disease comprising administrating to the patient a pharmaceutical composition of protein or polypeptide and colloidal particles.

(2) The state of the prior art:

The Merck manual indicates that there are plethora of disorders known, for example, Anorectal, foot and ankle, vascular, joint, mediatinal and pleural, arrhythmias and conduction, valvular, peripheral arterial to name just a few (see Merck manual, Disorders enclosed). Additionally, the Merck manual indicates that there are numerous numbers of diseases, for example, diverticular, bullous, tubulointerstital, prostate diseases, coronary artery diseases, viral skin diseases, inflammatory bowel disease, cystic kidney disease, Alzheimer's disease, Parkinson's disease, Wilson's disease to name just a few (see Merck manual, Diseases enclosed). For example, Alzheimer's disease according to the Merck manual is chronic, global, usually irreversible deterioration of cognition. The main types of Alzheimer's disease are: vascular dementia, Lewy body dementia, frontal-temporal dementias, and HIV-associated dementia (See Merck manual, "Dementia", Etiology and Classification, 2nd paragraph). Furthermore, Alzheimer's disease causes progressive cognitive deterioration and is characterized by senile plaques, beta-amyloid deposits, and neurofibrillary tangles in the cerebral cortex and subcortical gray matter (see Merck manual in Dementia under "Alzheimer's disease). Furthermore, the Merck manual indicates that most cases are sporadic, with late onset and unclear etiology (see Merck manual, "Alzheimer's disease", Etiology and Pathophysiology). Since symptoms, signs are similar to those of other dementia, distinguishing Alzheimer's disease from other dementias is difficult (see Merck Manual, "Alzheimer's disease", Symptoms, Signs, and Diagnosis). Furthermore, Mattson MP (Nature, 2004, 430: 631-639) indicates that the risk of Alzheimer's disease

(AD) dramatically increases in individuals beyond the age of 70 (see p. 631, left column, 1st sentence). The vast majority of cases of AD are sporadic, they do not run in families…molecular genetic analyses suggest that there are likely many genes that influence one's susceptibility to AD (see p. 633, left column, 2nd paragraph). Additionally, Mattson indicates that although drugs can temporarily improve memory, at present there are no treatments that can stop or reverse the inexorable neurodegenerative process (see abstract).

The art recognizes that there are countless different conditions, disorders and diseases, but does not provide how to determine the individuals who are susceptible to any disorder, condition or disease list provided by the Merck manual.

(3) The relative skill of those in the art:

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art:

Applicant's activity is based on the determination of predicting those who are susceptible to disorders, conditions and diseases. Since the activity is based on determining the patient population that is susceptible to disorders, conditions and diseases, the predictability in the art is low. This is due to the fact that the art has recognized that there are plethora of different conditions, disorders and diseases, but does not provide how to determine the individuals who are susceptible to any disorder, condition or disease list provided by the Merck manual. For example, not all elderly

people over 65 years of age suffer from Alzheimer's disease. Additionally, not everyone suffers from prostate cancer or AIDS.

As described above, Alzheimer's disease causes progressive cognitive deterioration and is characterized by senile plaques, beta-amyloid deposits, and neurofibrillary tangles in the cerebral cortex and subcortical gray matter (see Merck manual in Dementia under "Alzheimer's disease). Furthermore, the Merck manual indicates that most cases are sporadic, with late onset and unclear etiology (see Merck manual, "Alzheimer's disease", Etiology and Pathophysiology). Since symptoms, signs are similar to those of other dementia, distinguishing Alzheimer's disease from other dementias is difficult (see Merck Manual, "Alzheimer's disease", Symptoms, Signs, and Diagnosis). Furthermore, Mattson MP (Nature, 2004, 430: 631-639) indicates that the risk of Alzheimer's disease (AD) dramatically increases in individuals beyond the age of 70 (see p. 631, left column, 1st sentence). The vast majority of cases of AD are sporadic, they do not run in families…molecular genetic analyses suggest that there are likely many genes that influence one's susceptibility to AD (see p. 633, left column, 2nd paragraph). Additionally, Mattson indicates that although drugs can temporarily improve memory, at present there are no treatments that can stop or reverse the inexorable neurodegenerative process (see abstract).

The claims don't identify the type of disorder, condition or disease or the patient population, therefore, the claim implies that anyone can be protected against any disorder, condition or disease. However, the Applicant has not shown who will be susceptible to disorder, condition or disease and the types of disorder, condition or

disease. There are too many variables between the patient populations, thus, it clearly shows the unpredictability of the art.

(5) The breadth of the claims:

The claim is drawn to a method of treatment of a patient suffering from a disease comprising administrating to the patient a pharmaceutical composition of protein or polypeptide and colloidal particles.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples:

Although the specification provides guidance on how to make the composition and administer the compound, it is unclear as to when to administer the compound and the patient population. The specification discloses that hemophilia A are prone to frequent hemorrhages as a result of one or more misfunctions of the coagulation system (see p. 1, lines 6-7). The specification discloses that one of the causes of hemophilia is a shortage of Factor VIII in the blood and this problem can be treated with Factor VIII concentrates; however, in about 15% of the patients that occurrence results of Factor VIII neutralizing antibodies, so-called inhibitors, whereby a therapy with Factor VIII concentrates is hardly possible (see p. 1, lines 7-11). The specification discloses SCC injection of liposome-formulated G-CSF into mice, and pharmacokinetic parameters were calculated for each mouse (see p. 15, lines 8-13). Furthermore, the specification discloses the pharmacokinetic parameters following IV injection of Factor IX or

PEGylated liposome-formulated Factor IX into mice (see p. 15, line 15). The specification further discloses the biological activity of factor VIII that was formulated in-vivo with PEGylated liposomes by injection of liposomes 1 hour after the injection of unformulated factor VIII in hemophiliac mice. The specification discloses that the results indicate that the half-life and are under the curve of factor VIII that was formulated in vivo with PEGylated liposomes were higher than that of free FVIII (see Example 11). Additionally, the specification discloses that factor VIIa is generally used to treat hemophilia patients with inhibitors and to stop trauma bleeding. FVIIa formulated with PEGylated liposomes were injected into mice, and the rats were bled at various times post-injection and VFIIa activity was measured by a clotting assay and the results indicate that the half-life and are under the curve of FVIIa that was formulated in-vivo with PEGylated liposomes were higher than that of free FVIIa (see Example 13). There are not enough working examples for guidance. For example, as explained above, the specification only describes treatment of hemophilia, utilizing factor VIII, IX and VIIa.

The specification has not provided guidance in the way of a disclosure to how to determine individuals that need protection against any disorder, condition or disease. The specification discloses that the invention is particularly suited to patients previously diagnosed with prostate cancer. The specification discloses that the non-natural amino acid polypeptides, modified or unmodified, can be administered directly to mammalian subject by any of the routes normally used for introducing a polypeptide to a subject (see paragraph [0955]). Furthermore, the specification discloses that the effective amount of the formulation to be administered in the treatment or prophylaxis of disease

(including but not limited to cancers, inherited diseases, diabetes, AIDS, or the like) (see paragraph [0951]). As described above, Alzheimer's disease causes progressive cognitive deterioration and is characterized by senile plaques, beta-amyloid deposits, and neurofibrillary tangles in the cerebral cortex and subcortical gray matter (see Merck manual in Dementia under "Alzheimer's disease). Furthermore, the Merck manual indicates that most cases are sporadic, with late onset and unclear etiology (see Merck manual, "Alzheimer's disease", Etiology and Pathophysiology). Since symptoms, signs are similar to those of other dementia, distinguishing Alzheimer's disease from other dementias is difficult (see Merck Manual, "Alzheimer's disease", Symptoms, Signs, and Diagnosis). Furthermore, Mattson MP (Nature, 2004, 430: 631-639) indicates that the risk of Alzheimer's disease (AD) dramatically increases in individuals beyond the age of 70 (see p. 631, left column, 1st sentence). The vast majority of cases of AD are sporadic, they do not run in families…molecular genetic analyses suggest that there are likely many genes that influence one's susceptibility to AD (see p. 633, left column, 2nd paragraph). Additionally, Mattson indicates that although drugs can temporarily improve memory, at present there are no treatments that can stop or reverse the inexorable neurodegenerative process (see abstract). Since there are numerous different disorders, conditions (associated with different disorders and diseases) or diseases, there is not enough guidance to determine who is susceptible to certain disorder, condition or disease and when to administer the polypeptide.

There is no clear guidance as to how to determine the patient population, since not all people suffer from the same disorder, condition or disease. Since art recognizes

that there are countless different conditions, disorders and diseases, but does not provide how to determine the individuals who are susceptible to any disorder, condition or disease list provided by the Merck manual, more guidance is necessary.

(8) The quantity of experimentation necessary:

In order to treat a disease, a dosage, the subject and regimen must be identified. In order to ameliorate a disease symptoms or conditions, the end point of the treatment also needs to be identified. Since it is uncertain to predict the patient population who are susceptible for unknown disorder, condition or disease, and the Applicant have not provided the appropriate time frame at which the compound should be administered, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine if the compound would be effective in treating an adult, child, or an infant from all disorder, condition or disease.

Response to Applicant's Arguments

6. Applicant argues that "Applicants have elected the species G-CSF as the 'specific protein or polypeptide,' and multiple sclerosis as the disease for examination on the merits. Accordingly, Applicants note that pursuant to the Examiner's required election of species, the Examination of the present claims is limited to the elected species...Applicant argues that the claims are fully enabled for other diseases which may be treated by the proteins and polypeptides disclosed in the specification." Applicant further argues that "presently claimed subject matter is not concerned with a

new indication of treatment for a known protein, but rather with enhancing the therapeutic effect of known proteins for known disease by increasing their half-life in the blood stream." Applicant further argues that "the specification, figures, and experimental examples, provide ample guidance to the skilled artisan in view of the state of the art at the time the application was filed, to make and use the claimed invention without undue experimentation." Furthermore, Applicant argues that "Examiner's citation of Tompkins et al shows a nexus between the treatment of Multiple Sclerosis and the administration of a composition comprising G-CSF. Therefore, Applicant submits that the Examiner shows, on the record, that G-CSF is useful in the treatment of Multiple Sclerosis." Applicant further argues that "Declaration under 37 CFR 1.132 (Annex A and B) describes experimental results related to hemophilia, these results are representative of other diseases which may be treated with the compositions of the present claims; Applicant argues that Annex B may be used to provide a reasonable basis for the assumption that a composition comprising G-CSF may be used to treat other diseases for which G-CSF is known to be effective." Furthermore, Applicant argues "regarding neutropenia, two experiments were performed…white blood cell counts and differential counts of neutrophils, eosinophils, basophils, monocytes and lymphocytes were determined for each blood sample…the results of the experiments indicate that PEGLip-G-CSF is more effective than free G-CSF in enhancing white blood cells and neutrophils counts in both neutropenic rats and guinea pigs and the injection of PEGLip-G-CSF resulted in an increase of ~50% in white blood count AUC and absolute neutrophil

count AUC versus that of free G-CSF…PEGLip-G-CSF is more effective than free G-CSF in enhancing mobilization of stem cells into the peripheral blood."

7. Applicant's arguments have been fully considered but have not been found persuasive because the claims are broadly drawn to a method of treatment of a patient suffering from a disease. The treatment of disease, disorder or condition has no bearing on the compound or the composition. Furthermore, the art recognizes that there are plethora of disorders known, for example, Anorectal, foot and ankle, vascular, joint, mediatinal and pleural, arrhythmias and conduction, valvular, peripheral arterial to name just a few. The disorders, condition or diseases involve different cells, different organs of the body and different mechanisms. The therapeutic polypeptide that is utilized to treat one type of cancer may not treat other types of cancer. For example, a therapeutic polypeptide that treats prostate cancer or tumor may not treat other types of cancer such as lung, breast or leukemia. There are plethora of types of cancer. However, not one single therapeutic polypeptide treats all types of cancer. Furthermore, a person suffering from diabetes will have other diseases associated with the disease, such as heart condition, obesity, and high blood pressure. A therapeutic polypeptide, such as insulin, GLP-1, etc that are known for treating diabetes would not necessarily treat heart conditions, obesity or high blood pressure. Therefore, a therapeutic polypeptide to treat one disorder, condition or disease would not treat other disorder, condition or diseases. Applicant is correct that species of G-CSF and Multiple Sclerosis was elected in the election of species filed on June 11, 2007. However, to expedite the examination process, the Examiner has examined the broad aspects of the claims. If Applicant wants

to limit the scope of the claims solely to G-CSF and Multiple Sclerosis, the claims will be examined only to the elected species as Applicant's invention. Claims 47 and 50-51 are drawn to a method of treatment of a patient suffering from a disease comprising administrating a pharmaceutical composition of a protein or polypeptide and colloidal particle. The claims are not drawn to extending the life of the composition. In regards to Tompkins reference, there is a nexus between G-CSF and treating Multiple Sclerosis. However, Tompkins reference and the specification does not disclose treating ALL diseases using G-CSF or any other colloidal conjugated peptide/protein. Granulocyte colony-stimulating factor is a growth factor that stimulates the bone marrow to make more white blood cells. In regard to the 132 declaration, again the data is only directed to the white blood cells or neutrophils, those disease that are directed to blood disorder and G-CSF.

Furthermore, the therapeutic polypeptides are different amino acids in lengths: G-CSF (GenBank P35834) has 175 amino acid residues; GLP-1 (GenBank Accession No. NP_002045) has 185 amino acid residues; prothrombin (GenBank AAB24476) has 64 amino acid residues. Furthermore, the specification does not provide any examples as where these therapeutic polypeptides are modified or conjugated to the surface of PEG or liposome. The peptides listed above, G-CSF, GLP-1 and prothrombin each have multiple glutamic acid residues that may form bonds to the PEG or liposome; additionally, these peptides have multiple arginine and lysine residues that can form bonds to PEG or liposome.

Therefore, there are multiple sites where the therapeutic polypeptides can be conjugate to the PEG or liposomes. Furthermore, modification of therapeutic polypeptide incorporating the PEG or liposomes is not known to maintain the therapeutic effectiveness for ALL polypeptides. Thus, vast numbers of experimentation would be required to see if the polypeptide conjugated to PEG or liposome would have the same affect on certain diseases as the wild-type polypeptides. Again, the claimed invention is enabling for treating hemophilia, but the specification does not reasonably provide enablement for any other diseases, disorder or conditions.

New Rejection-35 U.S.C. 112, 1st

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 28-42 and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow

persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when

accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide and colloidal particles, the colloidal particle comprising 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer. The generic statements protein or polypeptide, protein or polypeptides that include a consensus sequence of S/T-X-L/I/V-I/V/Q/S-S/T-XX-E, where X may be any amino acid do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 28 is broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class

of peptide or a peptide-like molecule that can form peptide bonds, and make up the class of proteins or polypeptides. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives, variants or homologs. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules that can form peptide bonds, other synthetic peptide or peptide-like molecule, peptidomimetics or amino acid mimetics that can function as proteins or polypeptides that can bind to polymer or colloidal particles.

The specification is limited to the peptide or peptide-like molecules that belong to coagulation factors (Factor X, Factor VIIa, Factor IX, Factor X), granulocyte colony stimulating factor (G-CSF), granulocyte macrophage colony stimulating factor (GM-CSF), interferon-γ, and Glucagon like peptide-1 (GLP-1). The working examples 1-8 describe the liposome preparation, and binding the proteins/polypeptides to PEGlyated Liposomes. The examples disclose that the DSPE-PEG2000 binding to FVIII, and the

binding analysis was by Surface Plasmon Resonance measurement (comparing control liposomes with protein/peptide bound PEG-liposomes (see paragraphs [0043]-[0044]). Same experiments were performed on other recombinant and purified proteins: G-CSF, GM-CSF, Interferon and GLP-1 (see paragraph [0046]). Examples 9-10 disclose pharmacokinetics of liposome-formulated G-CSF and free G-CSF in mice. Example 11 describes the pharmacokinetics and biological activity of FVIII formulated PEGylated Liposomes in hemophilic mice in vivo (see paragraphs [0063]-[0064]). The specification does not describe any protein and polypeptide, or any other type of peptide or peptide-like molecule that functions a protein and polypeptide. Furthermore, the specification does not describe how the PEG-liposome is conjugated to the protein/polypeptide. Description of FVII, FIX, G-CSF, GM-CSF, IFN-γ, EPO, Human growth factor, Interferon-α2a, Interfereon-α2b, GLP-1 is not sufficient to encompass numerous other proteins and polypeptide that belong to the same genus. Furthermore, a protein or polypeptide having a consensus sequence S/T-X-L/I/V-I/V/Q/S-S/T-XX-E, where X may be any amino acid lead to many different peptide consensus sequences. For example, there are 20 naturally occurring amino acids, therefore X can be any 20 of the naturally occurring amino acids. Furthermore, there are three X's in the sequence. This lead to further variations to the consensus sequence. There are non-naturally occurring amino acids, such as D-amino acids, b-amino acids, g-amino acid and e-amino acids. When these are factored into the equation, there are even greater numbers of possibilities for the consensus sequence. Additionally, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Rejection-35 U.S.C. 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 28-32, 36-37 and 39-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Baru M (WO 99/55306, filed in the IDS 2/15/2006).

Baru teaches a pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide and substantially neutral colloidal particles. The particles comprise approximately 1-20 mole percent of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer which carries substantially no net charge. The protein or polypeptide is capable of

externally binding the colloidal particles, or is capable of binding polyethylene glycol and is not encapsulated in the colloidal particle (see abstract). Furthermore, the reference teaches that the term "proteins or polypeptides capable of externally binding said colloidal particles" includes proteins and polypeptides which, similarly to FVIII, binds to membranes comprising phosphatidylcholine:phosphatidylserine (PC:PS); non-limiting examples of such proteins are coagulation factors such as prothrombin, Factor X and Factor V (see p.7, lines 6-12, claims 18-19), which meets the limitations of claims 28-29, 32, 36-37 and 43. The reference further teaches that the colloidal particle has a mean particle diameter of between about 0.05 to about 0.4 microns, and approximately 0.1 microns (see claims 2-3), which meets the limitation of claims 30-31. It is noted that claim 30 has been rejected over the prior art, even though the reference does not disclose exact colloidal particle diameter range as claimed. However, both the claims and the reference utilize the term "about" when discussing the colloidal particle diameter. The term "about" allows for some tolerance in the ranges disclosed. In *In re Ayers*, the Federal Circuit held that "at least about 10%" was anticipated by a reference that disclosed "about 8%" because the term "about" allowed for some tolerance. *In re Ayers*, 154 F.2d 182, 185 (Fed. Cir. 1946). Similarly, in Johnson and Johnson v. W.L. Gore & Associates, Inc., the Court allowed for "about 1.2" to be inclusive of 1.0. See Johnson and Johnson v. W.L. Gore & Associates, Inc., 436 F.Supp. 704, 728-729 (Fed. Cir. 1977). Although about has never been confined to specific percentage of variability, the Johnson and Johnson decision at least implies that 16% variability is permissible when "about" is used (1.0/1.2 = ~16.6% variability). Thus, the term "about"

implicitly discloses some variability even though the specification may not literally cite this variability. Thus, the disclosure of a colloidal particle diameter of "about" 0.05 μm encompasses a diameter of "about" 0.03 μm, as claimed. The reference further teaches that the amphipathic lipid is a phospholipid from natural or synthetic sources (see claim 4), which meets the limitation of claim 32. The reference further teaches that the biocompatible hydrophilic polymer is selected from group consisting of polyalkylether, polylactic and polyglycolic acid families, and is a polyethylene glycol (see claims 6-7), which meets the limitations of claims 39-40.The reference further teaches that the polyethylene glycol has a molecular weight of between about 1000 to about 5000 daltons (approximately 2000 daltons) (see claims 8-9), which meets the limitations of claims 41-42.

12. Claims 28-29, 32-33 are 39-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Zalipsky et al (US Patent No. 6,586,002 B2).

13. Zalipsky et al teach a liposome composition comprising small, surface-bound effector molecules, and liposomes have a surface layer of hydrophilic polymer chains, for enhanced circulation time in the blood stream (see abstract), which meets the limitation of claim 28. The reference further teaches that polymer derivatized lipid is 1-25 percent, and for example, 5-10 mole percent PE derivatized with PEG 3500 polymer chains (see column 5, lines 57-58 and 62-63). The reference teaches that the liposome composition comprise liposomes, each having an outer layer of hydrophilic chains, and an effector molecule attached to the distal ends of said chain, and the effector molecule

is cytokine selected from the group consisting of interferons…GM-CSF, and G-CSF (see claims 1 and 4), which meets the limitations of claims 28 and 43. The reference further teaches that the liposomes have outer layer formed of hydrophilic polymer chains, PEG (see column 4, lines 38-40), and the effector is attached to the distal ends of the polymer in a portion of the derivatized vesicle-forming lipid (see column 4, lines 40-42). This indicates that the effector molecule (protein or peptide) is not encapsulated. Furthermore, the reference teaches that the vesicle-forming lipids of this type are preferably ones having two hydrocarbon chains, typically acyl chains, and a polar head group…phospholipids, such as phosphatidylcholine (PC), PE, phosphatidic acid (PA), phosphatidylinositol (PI), and sphingomyelin (SM) (see column 4, lines 61-67), one exemplary phospholipid is phosphatidylethanolamine (PE) (see column 5, lines 14-15), which meets the limitations of claims 29 and 32-33. The reference teaches that the preferred polymer is polyethyleneglycol (PEG), PEG chains having molecular weight between 1,000-10,000 daltons, more preferably 2,000 and 5000 daltons (see column 5, lines 18-20), which meets the limitation of claims 41 and 42.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654

/Anish Gupta/

Primary Examiner, Art Unit 1654